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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Mid-Atlantic Region

Food and Drug Administration
Waterview Corporate Center
10 Waterview Blvd., 3rd Floor
Parsippany, NJ 07054

Telephone (201) 331-2909

May 28, 1997

WARNING LETTER

Mr. Robert Miller
President
Direct Access Diagnostics
440 Route 22 East
Bridgewater, NJ 08807

File No: 97-NWJ-37

Dear Mr. Miller:

Investigators from this office conducted a postmarket inspection of your firm located in Bridgewater, New Jersey on March 24 - April 4, 1997, for the CONFIDE™ HIV Testing Service, PMA #BP90-003. The CONFIDE™ product is a biologic device as defined by Section 201(h) of the Federal Food, Drug and Cosmetic Act (Act).

The above-stated inspection revealed that this device is considered adulterated within the meaning of Section 501(h) of the Act, in that the methods used in, or the facilities or controls used for the manufacturing, packing, storage, or installation are not in conformance with the Good Manufacturing Practice (GMP) for Medical Device Regulation, as specified in Title 21, Code of Federal Regulations (CFR), Part 820, as follows:

1) Failure to validate changes to the Blood Absorbency Test utilized for incoming component testing and finished product testing. The NCCLS standard for this type of testing requires the use of fresh, whole blood with a 55% hematocrit. Your firm is utilizing frozen and thawed blood with no addition of cryoprotective agents. Since hemolysis occurs when blood is frozen, the hematocrit would decrease as a result of the freeze/thaw storage process. There is no documented evidence to substantiate this blood material is equivalent to 55% hematocrit fresh, whole blood for use in this significant testing method.

Based on the above, we are concerned about the accuracy of any validation studies that included frozen/thawed blood performed to determine whether the filter paper is compromised by moisture, compression and/or contaminants.

In your original PMA submission and several amendments to the original submission, you committed to following NCCLS guidelines for performing the quality control blood absorbency testing of the

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REVIEWED BY _____ 5/29/97
C.O. DATE

filter paper. The guidelines mandate the use of fresh, whole blood. While we note that subsequent to these commitments to use fresh, whole blood, you may have submitted information that indicated the use of frozen/thawed blood, you did not specifically highlight this change in methodology as required by the regulations concerning PMA amendments and supplements, found in 21 CFR 814.37 and 814.39.

2) Failure to establish and implement an adequate failure investigation program that would include an evaluation/review of device batch records for the test kit, testing of retain samples and questioning the user on their collection experience and test card handling.

The above-stated inspection also revealed that your device is misbranded within the meaning of section 502(t)(2) of the Act, in that your firm failed to submit information to the Food and Drug Administration as required by the Medical Device Reporting (MDR) Regulation, as specified in 21 CFR 803. Specifically, you failed to submit MDR reports to FDA after receiving information which reasonably suggest that the CONFIDE™ HIV Test Service may have reported false results to consumers on six occasions. These six complaints were received via telephone between September 16, 1996 and January 15, 1997.

Additionally, your firm's commitment to and implementation of the conditions of approval in your PMA approval letter, dated May 14, 1996 were evaluated by the Center for Biologics Evaluation and Research. It is noted that for the demographic survey instituted in February 1997 and provided to callers, the caller has the option to by-pass the survey completely. As a result, the demographic information required by the conditions of approval for your PMA is not being collected for all callers as evidenced by the fact that only 19 percent of the positive subjects and 26 percent of the negative subjects have participated in the optional demographic survey. Prior to the change to an optional survey, 43 percent of the positive subjects participated in the counselor-initiated demographic survey.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the FDA 483 issued at the closeout of the inspection may be symptomatic of serious underlying problems in our firm's manufacturing and quality

assurance systems. You are responsible for investigating and determining the causes of the violations identified by the FDA. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions.

Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts. Additionally, no premarket submissions for devices to which the GMP deficiencies are reasonably related will be cleared until the violations have been corrected. Also, no requests for Certificates For Products For Export will be approved until the violations related to the subject device have been corrected.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action being initiated by the Food and Drug Administration without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil penalties. In addition, approval of your PMA may be subject to withdrawal by the agency.

We are in receipt of your submitted response to the FDA483 observations, dated May 7, 1997. Our comments follow in the numerical order of the FDA483 observations:

1) We disagree with the rationale that either fresh or frozen/thawed blood is suitable for testing the filter paper used in the CONFIDE™ test card, based on [redacted] comments concerning the [redacted] NCCLS guidelines specifically state that fresh whole blood with 55% hematocrit is used for absorbency testing. If you choose to use lysed blood, you need to validate this test and arrive at specifications for this material. An effective validation effort should include a "worse case scenario" test designed to fail to meet specs if the filter paper is compromised.

2) This response is not complete. Volume retention of the filter paper is an important quality feature. Failure of the filter paper to retain the minimal amount of blood used in testing, which can not be visually determined, could possibly result in failure of the HIV test to detect antibodies. We acknowledge your commitment to retrospectively evaluate previously manufactured and released lots of test cards utilizing a

[redacted] variation of the volumetric test. However, while this is appropriate for retrospective validation purposes, there is no commitment to perform a QC test on each lot of finished product to determine if the volume retentive qualities of each finished product lot have been compromised.

An appropriate response for Observations 1 & 2 would include validation in conjunction with the development of a QC test method designed to detect when the filter paper has been compromised.

Responses to FDA483 Observations 3, 4, 5 & 7 appear to adequately address our concerns. While your response to Observation 6 appears adequate, the revised SOP (CS #100-001) was not included for our review.

Please notify this office in writing, within 15 working days of receipt to this letter, of the specific steps you have taken to correct this situation and include an explanation of each step taken to prevent the recurrence of similar deviations. If corrective action cannot be taken within 15 working days, state the reason for the delay and the timeframe within which corrections will be implemented.

Your reply should be directed to the New Jersey District Office, Food and Drug Administration, 10 Waterview Blvd, 3rd Floor, Parsippany, New Jersey, 07054, Attn: Mercedes B. Mota, Compliance Officer.

Sincerely,

Edward H. Wilkens

EDWARD H. WILKENS
Acting District Director
New Jersey District

**CERTIFIED MAIL -
RETURN RECEIPT REQUESTED**

MBM:np